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A case of cholinergic urticaria associated with acquired generalized hypohidrosis and abnormal neurological findings: association with incomplete Ross syndrome?

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MADAM, A 45-year-old man presented with a 15-year history of hypohidrosis, mainly on the left side of the body, and generalized urticarial rash upon physical exercise or exposure to hot water. These symptoms were associated with dizziness, palpitation and occasional heat intolerance in very hot weather, especially during summer. The patient had been treated with antihistamines and topical steroids without significant improvement.

Suspecting a diagnosis of cholinergic urticaria (CU), we performed a provocation test by subjecting the patient to 10 min of ergometer exercise, and found numerous small weals, 1–3 mm in diameter, on dry skin areas all over the body (Fig. 1a). A sweat test using the iodine-starch method revealed generalized pronounced hypohidrosis, especially on the left side of the trunk, and absent from the face, neck, axilla, palm and sole (Fig. 1b). Intradermal administration of a cholinergic agent (0.05 mL of 5% pilocarpine in distilled water) to the left forearm induced oedematous papules without sweating 15 min after the injection (Fig. 1c). An intradermal test for undiluted sweat was negative. The head-up tilt test revealed that the patient was positive for orthostatic hypotension. Sensorineural deafness on the left side was noted. As the association of hypohidrosis with neurological findings reminded us of Ross syndrome, we performed further neurological examinations. Cholinergic supersensitivity was noted in the form of enhanced miosis upon low-dose (0.125%) pilocarpine challenge. Slow nerve conductance velocity was also observed, but deep tendon reflex was normal.

Results of laboratory examinations (full blood count, renal, liver and thyroid function, fasting blood sugar and immunoglobulin levels) were all normal, and no autoantibodies were detected. Computed tomography scan and magnetic resonance imaging returned normal results. Histological examination of the hypohidrotic area on the right cubital fossa revealed atrophied sweat glands in low numbers with mild lymphocytic infiltration; examination of the anhidrotic area on the left cubital fossa revealed prominently atrophied sweat glands

(Fig. 1d). No hyperkeratosis in the horny cell layer or enhancing the sweat duct in the epidermis was observed. Therefore, we diagnosed this patient as having CU accompanied by acquired generalized hypohidrosis (AGH) with abnormal neurological findings.

CU is characterized by numerous small weals induced by increases in body temperature.¹ As in other types of urticaria, various pathogenetic mechanisms have been postulated including sweat allergy,² superficial obstruction of the acrosyringium by keratotic plugs,³ and AGH.⁴ Because of negativity for sweat allergy and keratotic plugs but positivity for hypohidrosis, our patient's CU is probably due to AGH.

In this case, the histology showed atrophied sweat glands in low numbers with lymphocytic infiltration in the absence of blockage of the acrosyringium, and intradermal administration of a cholinergic agent did not induce sweating. Therefore, one possible explanation for this disease is autoimmunity to sweat glands or to acetylcholine receptors on sweat glands. In addition, our patient was a candidate for oral steroid treatment because of the neurological findings. Therefore, he was treated with oral prednisolone (30 mg, 0.5 mg kg⁻¹ daily) for 2 weeks, whereupon the symptoms of CU disappeared and the hypohidrosis improved. In addition, the attenuated nerve conductance velocity, cholinergic hypersensitivity and dizziness have improved, although the sensorineural deafness has persisted.

This case was particularly intriguing because of the associated abnormal neurological findings: orthostatic hypotension, miosis upon pilocarpine challenge revealing cholinergic supersensitivity, left-side sensorineural deafness, and slow nerve conductance velocity. The association of hypohidrosis with neurological findings is reminiscent of Ross syndrome, which is characterized by tonic pupil with cholinergic supersensitivity, areflexia, and anhidrosis.⁵ To date, no case of CU associated with complete or incomplete Ross syndrome has been reported. The present case does not meet the diagnostic criteria for complete Ross syndrome, due to the normal deep tendon reflex and atrophic sweat glands, but may constitute an incomplete form.

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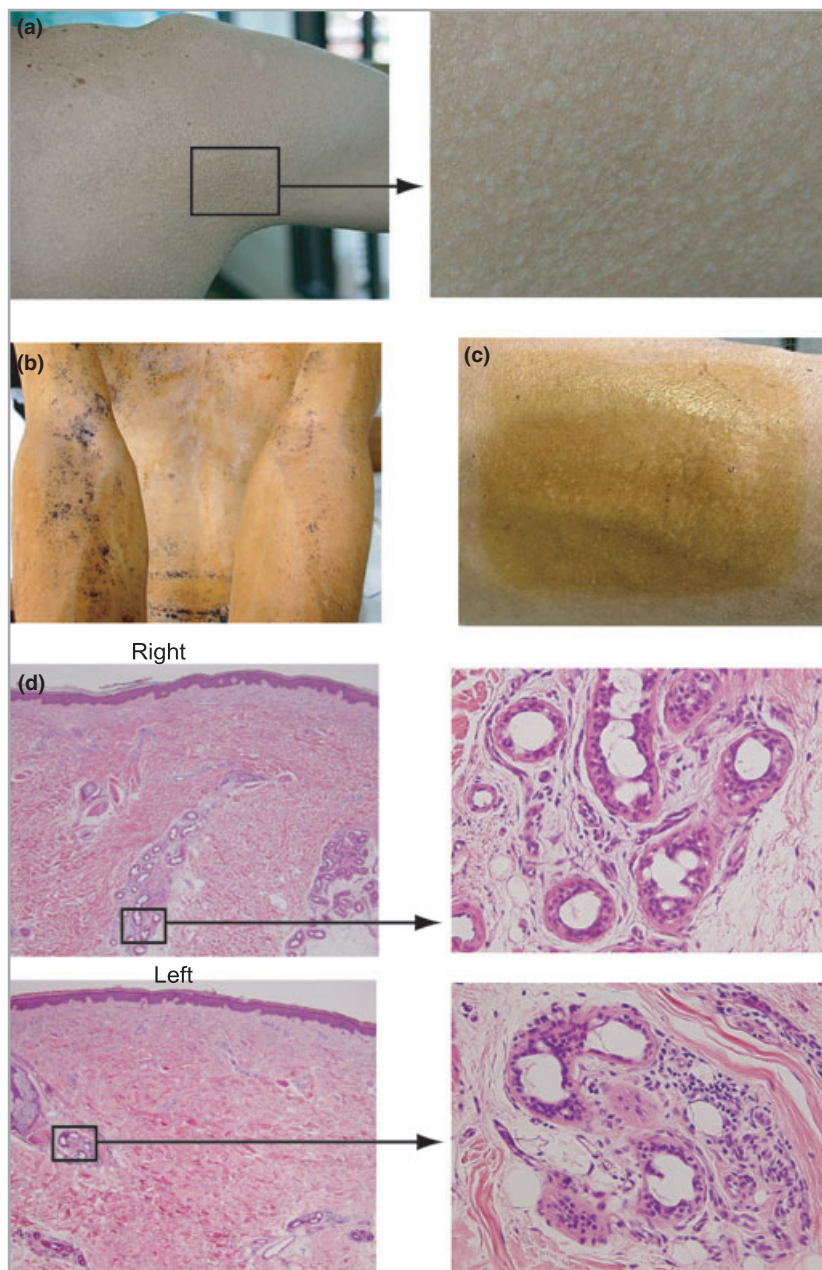


Fig 1. (a) Clinical appearance of the skin on the right shoulder. The right panel is a close-up of the area indicated by the square in the left picture. Numerous small wheals appeared after 10 min of ergometer exercise. (b) Sweat test (iodine-starch method). Hypohidrosis is seen mainly on the left side of the body. (c) Intradermal administration of a cholinergic agent induced oedematous papules without sweating. (d) Histology shows atrophic sweat glands with mild lymphocytic infiltration (haematoxylin and eosin).

References

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Key words: cholinergic urticaria, hypohidrosis, Ross syndrome

Conflicts of interest: none declared.